

A Summary of Research on the Effectiveness of Antidepressants and Psychotherapy

Michael Conner, PsyD

Summary

There is a significant gap between science and practice in the treatment of depression in America. Research internationally reports there is no valid or convincing evidence that antidepressants have a positive long term benefit with regard to depression or suicide rates. The majority of improvement attributed to antidepressants can be accounted for by factors of hope, desire, belief, fortuitous events, passage of time and behavioral changes made by patients over time. The response when treating children with antidepressants is minimal and less than the response reported in treatment of adults. A 12 week NIMH study demonstrates that antidepressants are more effective than psychotherapy and that psychotherapy combined with antidepressants can help in treating adolescents with depression. Another NIMH study of adults demonstrates that a 16 week trial of psychotherapy is superior both clinically and economically to 16 weeks of antidepressants. Based on these findings and prior research we may expect that psychotherapy of sufficient duration with children may also be more effective than antidepressants. Evidence that antidepressants can reduce suicidal behavior or attempts is weak and there is some evidence that suicide rates have increased since antidepressants came into use. Isolated research on the effectiveness of antidepressants claiming positive findings in adults and children may be misleading because many more studies show no statistically significant benefit. A majority of studies demonstrate that psychotherapy is effective, has a statistically significant benefit, and should be the first choice in treating mild, moderate and severe depression. Contrary to marketing and advertising claims, researchers and scientists have not demonstrated or claimed that depression is the result of a chemical imbalance or chemical insufficiency. There is no valid evidence that antidepressants correct any biochemical mechanism causing depression, or that such a mechanism exists. The benefits of antidepressants are not profound, lasting or predictable. Treatment using psychotherapy as a first line treatment appears to be a prudent, cost effective and a medically necessary course of action. Despite this, treatment recommendations over time by primary medical care to employ psychotherapy have declined. Based on research and practices internationally, it can be asserted that prescribing antidepressants without psychotherapy as a first-line treatment for depression may be negligent. Psychotherapy has withstood the test of time and has been demonstrated to be effective. Medications for depression have not.

In a 2002 review of research, Kirsch and Antonuccio (1) concluded that meaningful differences are lacking between antidepressants and placebos. In 1998 Kirsch and Sapirstein (2) as well as Kirsch and others (3) concluded the effects of antidepressant medication are weaker in children than in adults. Their conclusions regarding children are consistent with those found in all 7 prior reviews of the effects of antidepressants in depressed children (4,5,6,7,8,9,10).

In 2002, Kirsch and others (11) reviewed all applications for antidepressant medications to the US Food and Drug Administration. An examination of all submitted trials of newer antidepressant medications, found that the benefit of antidepressant medications was much smaller when all studies were considered rather than when only the published studies.

In 2004, the National Institute for Mental Health (NIMH) (12) conducted a clinical trial of 439 adolescents with major depression at 13 sites nationwide. The study compared cognitive-behavioral therapy (CBT) with Prozac which is the only antidepressant approved by the Food and Drug Administration for use in children and adolescents. At 12 weeks the combination of medication and psychotherapy was deemed the most effective treatment. Compared with placebo, the combination of Prozac with CBT was statistically significant using the Children's Depression Rating Scale-Revised. Compared with Prozac alone and CBT alone, treatment using Prozac with CBT was superior. It was concluded that Prozac alone was a superior treatment to CBT alone. Rates of response for Prozac with CBT were 71%; Prozac alone, 60%; CBT alone, 43%; and placebo, 35%. This study suggests that approximately 26% of people placed on Prozac alone will benefit by the 12th week. But, 37% of the people placed on psychotherapy and Prozac will benefit by the 12th week.

In this same study, clinically significant suicidal thinking, which was present in 29% of the sample at baseline, improved significantly in all 4 treatment groups. Prozac with CBT showed the greatest reduction. Seven (1.6%) of 439 patients attempted suicide and there were no completed suicides. The combination of Prozac with CBT offered the most

favorable tradeoff between benefit and risk for adolescents with major depressive disorder. When the investigators used a broader definition of harm-related events to include suicidal and nonsuicidal behavior such self-harm, increase in suicidal ideas, or thoughts or acts of harm to others or property, they found a significantly higher rate in the Prozac groups (13).

In 2004 Kirsch and Antonuccio (14) testified before the Food and Drug Administration stating there are a total of 12 published randomized clinical trials (RCT) in the entire world literature of treating children with antidepressants. Eight of these 12 trials failed to find any significant benefit of medication over inert placebo. Only 4 of the RCTs claimed significant differences between drug and placebo, and those did so only on clinician rated measures, not patient rated measures. Three of the clinical trials did not report means and/or standard deviations, leaving 9 for a meta-analysis. When these nine studies are combined the improvement attributed to placebo was 87%. Overall, this means that no more than 13% of people who improved actually benefited from antidepressants. No more than 25 % of people who improved responded to SSRIs like Prozac. This meta-analysis indicates that Tricyclic Antidepressants (TCAs) have no significant pharmacological effect on depression in children. In effect, 75% of the SSRI response and 97% of the TCA response is placebo or consequences that are associated with the passage of time. While the effects of Selective Serotonin Reuptake Inhibitors (SSRIs) like Prozac are statistically significant, there was no evidence in these studies that the use of these drugs was clinically significant.

In 2004, Pampallona and others (15) conducted a meta-analysis and found that combined psychotherapy and medications with adults were more effective than psychotherapy alone. They also found that psychotherapy can help keep patients in drug therapy. They recommended further research to explore interventions that might serve as a “treatment compliance mechanism” for drug therapy.

In 2005, after an extensive review, Arroll and others (16) found only 15 studies based in primary care that met inclusion criteria and provided evidence for the comparative efficacy of tricyclics and SSRIs vs placebo. Adult patients responded to 56% to 60% to antidepressants compared with 42% to 47% for placebo. 40 to 44% did not improve at all. As such, only 13 to 18% of adults actually benefited from an antidepressant. This systematic review is the first comparing antidepressants with placebo for treatment

of depression identified in primary medical care. Both TCAs and SSRIs were considered effective for adults but the effect was small. This comprehensive review is also the first to show that low-dose TCAs are effective in primary care. As such, prescribing a tricyclic or SSRI antidepressant in primary care is a more effective clinical activity than prescribing placebo - but only 13 to 18% more than placebo. While statistically significant, this is not a profound effect.

In 2005, during a study of 240 patients, DeRubeis and others (17) reported that cognitive therapy worked as well as a popular antidepressant for moderate to severe depression. In the study, patients on medication got better quicker. At eight weeks, the response rate was 50 percent for Paxil, 43 % for cognitive therapy and 25 % for placebo. But by 16 weeks, 58 % of patients in both treatment groups were feeling better. Patients who got 16 weeks of cognitive therapy also had about the same relapse rate a year later as people who took an antidepressant the whole time. If people quit taking Paxil after 16 weeks, their relapse rate was twice that of therapy patients who had 16 weeks of psychotherapy. These findings suggest that psychotherapy is more effective and will cost less in the long run.

Following their study, and during an interview with the Philadelphia Inquirer on April 4, 2005, DeRubeis and Hollon (18) stated that the American Psychiatric Association should change its treatment guidelines for moderate to severe depression, which currently call for antidepressants as the first-line treatment.

In 2005, Moncrieff and Kirsch (19) reported that longitudinal follow-up studies show very poor outcomes for people treated with antidepressants for depression both in hospital (20) and in their community, (21), and most importantly, that the overall prevalence of depression is rising despite increased use of antidepressants (22). “Two studies that prospectively assessed outcome in depressed patients treated naturalistically by general practitioners and psychiatrists found that people prescribed antidepressants had a slightly worse outcome than those not prescribed them, even after baseline severity had been taken into account (23,24).” No comparable studies could be found that showed a better outcome in people prescribed antidepressants in the long term.

In their 2005 review Moncrieff and Kirsch (19) also found that some authors have suggested a causal association between increased antidepressant

prescribing since 1990 and reduction of overall suicide rates observed in some countries. However, other researchers have pointed out that drops in overall suicide rates started long before this period, and suicide rates have increased in some age groups and some countries despite increased antidepressant prescribing. Meta-analyses of data from controlled trials have not found reduced rates of suicide or suicidal behavior in drug use compared with placebos. The positive effect of antidepressants on suicide rates in the long term is unclear. Moncrieff and Kirsch also conclude that recent meta-analyses show SSRI's have no clinically meaningful advantage over placebo. Claims that antidepressants are more effective in more severe cases of depression have little evidence to support them.

Antidepressants: Reality or Myth ?

Why do professionals and the public believe that antidepressants are an effective first-line treatment approach? There are a number of research designs and methodology errors that can explain isolated findings as well as why research can be perceived as positive by professionals and lay people. John (25) described how false findings may be the majority or the vast majority of published research. It can be proven that most positive research findings are false. For example, the probability that any research finding is true depends on the prior probability that it is true. Isolated positive findings may in fact be false if the preponderance of prior studies is negative. Negative findings from single studies are generally not published. Therefore, patients, professionals and researchers can be misled.

John describes how distorted reporting and weak definitions of improvement are among the most typical forms of bias. For example, an ordinal rating system is typically used to measure response to medications. A person with a score of 40 may be more depressed than a score of 20 but this does not mean they are twice as depressed. Other biases include the researcher's profession, career interests, funding sources, size of the study and the complexity of disorder being measured.

In 2005, Lacasse and Leo (26) provide evidence and present expert opinions that there is no evidence to support widely promoted claims regarding the cause of depression, the effectiveness of antidepressants, and how antidepressants work. Lacasse and Leo cite studies, experts and leading scientists who conclude there is insufficient evidence to support a belief that depression is the result of a serotonin deficiency and that drugs like Prozac can

correct this problem. Furthermore, there is no valid evidence to support the conclusion that depression is the result of a "chemical imbalance."

Lacasse and Leo suggest that despite a lack of evidence, and even evidence to the contrary, the pharmaceutical industry markets and educates the public, schools and health care describing a cause and treatment for depression that is not substantiated by research, science and expert opinion.

Does Psychotherapy Work?

In one of the first reviews of psychotherapy outcomes, Hampe and others (27) in 1973 evaluated the progress of 62 phobic children 1 and 2 yrs after termination of treatment or waiting period. 80% were either symptom free or significantly improved; only 7% still had a severe phobia. Successfully treated patients tended to remain symptom free and to be free from other deviant behaviors as well. 60% of the failures at termination continued to receive treatment and most were symptom free 2 yrs later.

Smith and Glass (28) in 1977 analyzed the results of 375 controlled evaluations of psychotherapy and counseling. The findings provide convincing evidence of the efficacy of psychotherapy. On the average, the typical therapy client is better off than 75% of untreated individuals. Few important differences in effectiveness could be established among very different types of psychotherapy.

In 1979, Lesser (29) reviewed traditional psychotherapy outcome studies, which show that psychotherapy is more effective than placebo, long-term psychotherapy is as effective as brief, and limited hard data are available as to the effectiveness of the psychotherapies used. Cost-benefit studies show that brief psychotherapy is cost effective, while long-term psychotherapy clearly reduces hospitalization costs.

In 1981, Andrews and others (30) analyzed the results of 81 controlled psychotherapy trials. The condition of the typical patient after treatment was better than that of 77% of untreated controls measured at the same time, and the rate of relapse in the first 2 years was small.

Also in 1981, Tramontana (31) describes and critically evaluate studies on individual, group, and family therapy that were published from 1967 through 1977. Five were judged as exemplary in methodological scope and rigor. The greater weight of available evidence on adolescents does point toward the superiority of psychotherapy over no-therapy conditions, with the median rate of positive outcome

with psychotherapy being approximately 75%, compared with a rate of 39% without psychotherapy.

In 1982, Smith (32) applied meta-analysis to 475 studies of the effectiveness of psychotherapy and 112 studies of the comparative effects of psychotherapy and psychoactive drugs. Their analysis showed that psychotherapy is effective in enhancing psychological well-being, regardless of the way it is measured by researchers. Drug therapy, while combining well with psychotherapy, is not more effective than psychotherapy alone.

In 1985, Casey and others (33) examined 75 studies. Results show that therapy with children was similar in effectiveness to therapy with adults; treated children achieved outcomes about two-thirds of a standard deviation better than untreated children. Although behavioral treatments appeared to be more effective than non-behavioral treatments, this apparent superiority was due largely to the types of outcome and target problems included in behavioral studies.

In 1986, Howard and others (34) analyzed data based on more than 2,400 patients, covering a period of more than 30 yrs of research. Results indicated that by 8 sessions approximately 50% of patients were measurably improved, and approximately 75% were improved by 26 sessions.

In 2002, Wampold and others (35) conducted a meta-analysis of studies that compared Cognitive Therapy (CT) to 'other therapies' in an earlier meta-analysis, except that in this meta-analysis "other therapies" were classified as bona fide and non-bona fide. Bona fide treatments were defined as treatments with therapeutic rationale for depression. The benefits of CT were found to be approximately equal to the benefits of bona fide non-CT and behavioral treatments, but superior to non-bona fide treatments. The results of this study support the conclusion that all bona fide psychological treatments for depression are equally efficacious.

In 2003 Hubble, Duncan and Miller (36) published a comprehensive review and analysis of psychotherapy process and outcomes. They determined the proportion of improvement in psychotherapy was the result of (a) the techniques used, 15%, (b) patient expectations and placebo, 15%, (c) the relationship with a therapist (30%) and (d) environmental and patient resources such as social support, fortuitous events, and patient strengths, 40%. Placebo and expectancy effects in psychotherapy are less than those found in treatment with antidepressants. Placebo and patient expectation are

generally defined as hope, desire or a belief that change will occur.

In an extensive review of research, Hunsley (37) in 2003 outlined how "empirical evidence has demonstrated that psychological interventions can effectively treat a wide range of child and adult health problems. The focus of this review is on cost issues associated with psychological interventions, including cost-effectiveness and cost offset (i.e., a reduction in health care costs attributable to effective intervention)." Hunsley concluded that evidence thus far has demonstrated "that psychological interventions can be more cost-effective than optimal drug treatment. For example, although having comparable effectiveness, cognitive-behavioral treatments for panic disorder and for depression have been estimated to cost approximately one-third less than pharmacological treatment. Most important he points out that a recent meta-analysis of 91 research studies published between 1967 and 1997 found that average health care cost savings due to psychological intervention were in the range of 20–30% across studies, and 90% of the studies reported evidence of a medical cost offset. As of 2003 there is overwhelming evidence that psychological treatments (a) can be cost-effective forms of treatment and (b) have the potential to reduce health care costs, as successfully treated patients typically reduce their utilization of other health care services."

Hunsley also describes how many effective psychological services result in a net cost benefit to health care systems. This is how it should be in any health care system that truly aims to improve the health of the population through effective treatments to reduce pain, distress, suffering, and disability. "Psychological interventions work for an enormous range of health problems and, although attempts to promote greater access to these services must include arguments based on cost-effectiveness and cost offsets, they should not be (and have not been) totally reliant on economic arguments."

Treatment Issues in America

In 2000, Berndt and others (38) examined 2222 persons employed as data processors at multiple sites nationwide. The average daily productivity of employees with 1 or more mental disorders for which they were receiving treatment was no different from that of employees with no mental disorders. Despite this finding, which suggests the effectiveness of treatment, the cost data were striking: "controlling for age and sex, employees with more than 1 mental health disorder have total medical expenditures about

10 times those of employees with no mental disorder." When considered alone, the expenditures associated with 4 solo mental disorders. Anxiety, depression, adjustment disorders, and other mental disorders (mainly substance abuse) were similar in magnitude to one another, each averaging about 4.5 times the total medical expenditures of those with no mental disorder.

Depression is the world's fourth most prevalent health problem (39) costing the United States \$30 to \$50 billion in lost productivity and direct medical costs each year (40,41). Persons who are depressed miss work because of illness at twice the rate of the general population (42). Health service costs are 50% to 100% greater for depressed patients than for comparable patients without depression. These increased costs are caused by higher medical utilization, not by specialty mental health care (43, 44). Additional costs associated with depression include impaired concentration, failure to advance in educational and vocational endeavors, increased substance abuse, impaired or lost relationships, and suicide (45, 46).

In 2000, the Agency for Health Care Policy and Research (AHCPR), the Veterans Health Administration/Department of Defense (VHA-DOD), and the American Psychiatric Association (APA) published evidence-based recommendations for depression treatment. Pharmacotherapy and psychotherapy (combination treatment) are recommended when treating moderate to severe depression. When the depression is mild to moderate and the patient is motivated to work on psychological and interpersonal issues, psychotherapy is warranted (48, 49, 50).

Schulberg and other (39) in 1999 concur with the AHCPR guidelines and concluded that referral to a mental health professional should be a part of depression treatment, especially when patients exhibit severe depressive symptoms (e.g., suicide risk; comorbid medical, psychiatric, or substance use disorder; or failure to respond to appropriate treatment).

In his review of "cost offset" in the treatment of depression, Pomerantz (51) in 2001 stated that "antidepressants do not cure the 'medicalization of life', which is something Thomas Szasz warned about more than a quarter of a century ago. Furthermore, antidepressants do not alleviate problems of living (e.g., pain associated with chronic arthritis or diabetic neuropathy, low self-esteem, a rejecting spouse) or

completely eradicate the somatic preoccupations of either patients or prescribers."

In 2002, Olfson and others (52) found that between 1987 and 1997 there was a marked increase in the proportion of the population who received outpatient treatment for depression. Treatment was characterized by greater involvement of physicians, greater use of medications, and expanding availability of third-party payment, but fewer outpatient visits and less use of psychotherapy. The proportion of treated individuals who used antidepressant medications increased from 37.3% to 74.5%, whereas the proportion who received psychotherapy declined significantly from 71.1% to 60.2. The average number of depression treatment visits per patient declined significantly from 12.6 to 8.7 per year. An increasingly large proportion of patients, 68.9% to 87.3%, were treated by physicians for their condition, and treatment costs covered by third-party payers increased from 39.3% to 55.2%.

In their 2005 review, Keesler and other (53) found that no significant changes occurred between 1990-1992 and 2001-2003 in suicidal ideation, plans, gestures, or attempts, whereas plans among ideators increased significantly from 19.6% to 28.6%, and conditional prevalence of gestures among planners decreased significantly from 21.4% to 6.4%. Treatment increased dramatically among ideators who made a gesture from 40.3% to 92.8% and among ideators who made an attempt from 49.6% to 79.0%. But despite a dramatic increase in treatment, no significant decrease occurred in suicidal thoughts, plans, gestures, or attempts in the United States during the 1990s.

In 2005, Robinson and others (48) found that primary care physicians as a whole initiated antidepressant interventions more frequently than any other treatment for depression. In particular, the physicians prescribed antidepressants for an average of 52% of their newly diagnosed depressed patients, combination treatment (pharmacological and psychological) for an average of 27% of the patients, and psychotherapy alone for only 4% of the depression patients.

Discussion

Depression in children and adults is without question a serious problem that has a significant negative impact on health care and the economy of the United States. In response to this public health problem, antidepressants are the first line treatment despite evidence that psychotherapy is more effective and less expensive in the long run.

There is also reason to suspect that the treatment of depression by physicians has not had a profound or positive effect on reducing suicidal behavior. More research is necessary.

In the United States, physician prescribing of antidepressants for depression is increasing while referrals for psychotherapy are decreasing. This is the reverse of what might be expected since there is limited and minimal evidence that antidepressants are effective with adults and children. Psychotherapy appears to be effective and more effective for both adults and children than antidepressants. Practically speaking, all competent psychotherapies for depression are equally effective.

How then can our health care system recommend medications without psychotherapy knowing that medications do not alleviate problems in living? Some possible reasons for the higher use of antidepressants may include (a) the introduction of SSRIs such as Prozac that have fewer side effects than tricyclics, (b) aggressive pharmaceutical industry advertising, (c) research publication bias, (d) errors in research methodology, (e) an increased level of screening for depression, (f) third party reimbursement for medications, and (g) a greater number of physicians willing to treat depression in primary medical care.

There is clear evidence that antidepressants can help some patients. There is sufficient evidence to suggest that competent psychotherapy should be the first line treatment for depression. There is also evidence that psychotherapy alone can be prescribed for severe cases of depression and that a combination of psychotherapy and antidepressants can be prescribed for severe and unresponsive patients.

These findings suggest that there is a significant gap between science and treatment of depression in America. Current guidelines and recommendations for the treatment of depression in the United States should be revised in light of research findings internationally.

References

- (1) Kirsch, I. & Antonuccio, D. Antidepressants Versus Placebos: Meaningful Advantages Are Lacking, *Psychiatric Times* 2002 Vol. XIX, Issue 9.
- (2) Kirsch I. & Sapirstein G. (1998), Listening to Prozac but hearing placebo: A meta analysis of antidepressant medication. *Prevention & Treatment* 1: Article 0002a. Available at: <http://www.journals.apa.org/prevention/volume1/pre0010002a.html>
- (3) Kirsch I., Moore T., & Scoboria A., Nicholls S. The emperor's new drugs: an analysis of antidepressant medication data submitted to the U.S. Food and Drug Administration. *Prevention & Treatment* 2002 5: Article 23. Available at: <http://journals.apa.org/prevention/volume5/pre0050023a.html>
- (4) Ambrosini, P.J., Bianchi, M.D., Rabinovich, H., & Elia, J. Antidepressant treatment in children and adolescents: I. Affective Disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, 1993 32, 1-6.
- (5) Duvjone, V.F., Barnard, M.U., & Rapoff, M.A. Pharmacological and cognitive-behavioral approaches in the treatment of childhood depression: A review and critique. *Clinical Psychology Review*, 1995 15, 589-611.
- (6) Fisher, R.L. & Fisher, S. Antidepressants for children: Is scientific support necessary? *The Journal of Nervous and Mental Disease*, 1996, 184,99-102.
- (7) Hazell, P., O'Connell, D., Heathcote, D., Robertson, J., & Henry, D. Efficacy of tricyclic drugs in treating child and adolescent depression: a meta-analysis. *British Medical Journal*, 2005 310, 897-901.
- (8) Kastelic, E.A., Labellarte, M. J., & Riddle, M.A. (2000). Selective serotonin reuptake inhibitors for children and adolescents. *Current Psychiatry Reports*, 2, 117-123.
- (9) Michael, K.D. & Crowley, S.L. How effective are treatments for children and adolescent depression? A meta-analytic review. *Clinical Psychology Review*, 2002 22, 247-269.
- (10) Sommers-Flanagan, J. & Sommers-Flanagan, R. Efficacy of antidepressant medication with depressed youth: What psychologists should know. *Professional Psychology: Research and Practice*, 1996, 27, 145-153.
- (11) Kirsch I., Moore T., Scoboria A., & Nicholls S. The Emperor's new drugs: An analysis of antidepressant medication data submitted to the US Food and drug administration. *Prep Treat* 2002;5:1522-1534.
- (12) National Institute of Mental Health Research on Treatment for Adolescents with Depression Study (TADS): Combination Treatment Most Effective in Adolescents with Depression. (February 8, 2005) National Institute of Mental Health. Retrieved from the World Wide Web:

<http://www.nimh.nih.gov/healthinformation/tads.cfm>

- (13) Moyer, P. Combination SSRI and CBT Most Effective for Adolescent Depression. AACAP 51st Annual Meeting: Abstract 49b. Presented Oct. 23, 2004.
<http://www.medscape.com/viewarticle/491998>
- (14) Food and Drug Administration Testimony of Dr. Irving Kirsch and Dr. David Antonuccio on the Efficacy of Antidepressants with Children. (February 2, 2004). Retrieved from the World Wide Web:
<http://www.ahrp.org/risks/SSRI0204/KirschAntonuccio.php>
- (15) Arroll, B.; Macgillivray, S.; Ogston, S.; Reid, I., MRCPsych; Sullivan, F.; Williams, B.; & Crombie, I. (2005) Efficacy and Tolerability of Tricyclic Antidepressants and SSRIs Compared with Placebo for Treatment of Depression in Primary Care: A Meta-Analysis. *Annals of Family Medicine*. 2005;3(5):449-456.
- (16) Pampallona S, Bollini P, Tibaldi G, & Kupelnick B, Munizza C: Combined pharmacotherapy and psychological treatment for depression: a systematic review. *Archives General Psychiatry* 2004; 61:714-719
- (17) DeRubeis, R., Hollon, S. Amsterdam, J.; Shelton, R.; Young, P.; Salomon, R.; O'Reardon, J.; Lovett, M.; Gladis, M; Brown, L.; & Gallop, R.. Cognitive Therapy vs Medications in the Treatment of Moderate to Severe Depression *Archives General Psychiatry*, April 2005; 62: 409-416
- (18) Study: Cognitive Therapy As Effective As Drug in Treating Depression. Retrieved from Mental Health Foundation on the web January 21, 2006
http://www.mentalhealth.org.uk/profile/news.cfm?pagecode=PMSTTTNE&areacode=mh_talking_treatments_news&id=7624
- (19) Moncrieff, J. & Kirsch, I. Efficacy of Antidepressants in Adults. *British Medical Journal* 2005 331:155-157 ,
doi:10.1136/bmj.331.7509.155
- (20) Tuma T. Outcome of hospital treated depression at 4.5 years. An elderly and a younger cohort compared. *British Journal Psychiatry* 2000;176:224-8.
- (21) Goldberg D., Privett M., Ustun B., Simon G., & Linden M. The effects of detection and treatment on the outcome of major depression in primary care: a naturalistic study in 15 cities. *British Journal General Practices* 1998;48:1840-4.
- (22) Fombonne E. Increased rates of depression: update of epidemiological findings and analytical problems. *Acta Psychiatrica Scandinavica* 1994;90:145-56.
- (23) Brugha T., Bebbington P., MacCarthy B., Stuart E., & Wykes T. Antidepressants may not assist recovery in practice: a naturalistic prospective survey. *Acta Psychiatrica Scandinavica* 1992; 86:5-11.
- (24) Ronalds C, Creed F, Stone K, Webb S, & Tomenson B. The outcome of anxiety and depressive disorders in general practice. *British Journal Psychiatry* 1997;171:427-33.
- (25) John, P. Why Most Published Research Findings Are False. *PLoS Med* 2005 2(8): e124
- (26) Lacasse JR, Leo J Serotonin and Depression: A Disconnect between the Advertisements and the Scientific Literature. *PLoS Med* 2005 2(12): e392
- (27) Hampe, E.; Noble, H.; Miller, L.; Barrett, & Curtis L. Phobic children one and two years post-treatment. *Journal of Abnormal Psychology*; 1973 Dec Vol. 82(3) 446-453
- (28) Smith, Mary-L.; Glass, & Gene V. Meta-analysis of psychotherapy outcome studies. *American Psychologist*; 1977 Sep Vol 32(9) 752-760
- (29) Lesser, A. Psychotherapy, benefits and costs. *Psychiatric Journal of the University of Ottawa*; 197,9 Jun Vol 4(2) 191-196
- (30) Andrews, Gavin; Harvey, & Robin. Does psychotherapy benefit neurotic patients? A reanalysis of the Smith, Glass, and Miller data. *Archives of General Psychiatry*; 1981 Nov Vol 38(11) 1203-1208
- (31) Tramontana, M. Critical review of research on psychotherapy outcome with adolescents: 1967-1977. *Annual Progress in Child Psychiatric and Child Development*; 1981 521-550
- (32) Smith, Mary L. What research says about the effectiveness of psychotherapy. *Hospital and Community Psychiatry*; 1982 Jun Vol 33(6) 457-461
- (33) Casey, Rita J.; Berman, Jeffrey S. The outcome of psychotherapy with children. *Psychological Bulletin*; 1985 Sep Vol 98(2) 388-400
- (34) Howard, K.; Kopta, S. Mark; Krause, Merton, S.; Orlinsky, David-E. The dose-effect relationship in psychotherapy. Special Issue: Psychotherapy

- research. *American Psychologist*; 1986 Feb Vol 41(2) 159-164
- (35) Wampold BE, Minami T, Baskin TW, Callen TS: A meta-(re)analysis of the effects of cognitive therapy versus “other therapies” for depression. *Journal Affective Disorders* 2002; 68:159–165
- (36) Hubble, M. A., Duncan, B. L. & Miller S. D. (2002) *The Heart and Soul of Change*. American Psychological Association.
- (37) Hunsley, J. (2003) Cost-Effectiveness and Medical Cost-Offset Considerations in Psychological Service Provision. *Canadian Psychology*, Vol. 44, No. 1, 61-73
- (38) Berndt E., Bailit H., Keller M., et al. Health use and at-work productivity among employees with mental disorders. *Health Affairs*. 2000;19:244-255.
- (39) Schulberg H., Katon W., Simon G., Rush A. Best clinical practice: Guidelines for managing major depression in primary medical care. *Journal Clinical Psychiatry* 1999; 60 Suppl 7: 19-26.
- (40) Greenberg P., Finkelstein S., Berndt E. Calculating the workshop cost of chronic disease. *Business Health* 1995; 13: 27-28, 30.
- (41) Rice D., Miller L. Health, economics, and cost implications of anxiety and other mental disorders in the United States. *British Journal Psychiatry Supplement* 1998; 34: 4-9.
- (42) Von Korff M., Katon W., Unutzer J., Wells K., Wagner E.. Improving depression care: barriers, solutions, and research needs. *Journal Family Practice* 2001; 50: E1.
- (43) Henk H, Katzelnick DJ, Kobak KA, Greist JH, Jefferson JW. Medical costs attribution to depression among patients with a history of high medical expenses in a health maintenance organization. *Arch Gen Psychiat* 1996; 53: 899-906.
- (44) Simon G., VonKorff M. Recognition, management, and outcomes of depression in primary care. *Archives Family Medicine* 1995; 4: 99-105.
- (45) Pincus H., Pettit A. The societal costs of chronic major depression. *Journal Clinical Psychiatry* 2001; 62 Suppl 6: 5-9.
- (46) Greden J. The burden of recurrent depression: causes, consequences, and future prospects. *Journal Clinical Psychiatry* 2001; 62 Suppl 22: 5-9.
- (47) Robinson, D., Geske J., Prest L., & Barnacle R., Depression Treatment in Primary Care. *Journal American Board Family Practice*. 2005; 18 (2): 79-86.
- (48) HCPR Depression Guideline Panel. Clinical Practice Guideline Number 5. Depression in primary care. Volume 2: treatment of major depression. AHCPR publication no. 93-0550. Rockville (MD): Agency for Health Care Policy and Research, Public Health Services, US Department of Health and Human Services; 1993.
- (49) American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder. Washington DC: American Psychiatric Association; 2000. Available at: http://www.psych.org/psych_pract/treatg/pg/Depression2e.book.cfm
- (50) The Management of Major Depressive Disorder Working Group. Clinical practice guideline for the management of major depressive disorder in adults, version 2.0. Washington DC: Veterans Health Administration/Department of Defense; 2000.
- (51) Pomerantz, J. Is There a Cost Offset in Treating Depression for High-Utilizing Medical Patients? (Part 2 of 2) *Drug Benefit Trends* 13(4):2bh-3bh, 2001
- (52) Olfson M., Marcus S., Druss B., Elinson L., Tanielian T., & Pincus H. National trends in the outpatient treatment of depression. *JAMA* 2002; 287: 203-9.
- (53) Kessler, Ronald.; Berglund, Patricia.; Borges, Guilherme.; Nock, Matthew.; & Wang, Philip. Trends in Suicide Ideation, Plans, Gestures, and Attempts in the United States, 1990-1992 to 2001-2003. *JAMA*. 2005;293:2487-2495.

Michael Conner is a psychologist who serves on the Board of Directors for Mentor Research Institute in Portland Oregon, USA. Mentor Research Institute is a 501c3 charitable nonprofit research, training and consumer information organization founded in 1996.

This paper is based entirely on research published by the professionals cited in the References. It is a synthesis of extensive research and expert opinions selected by the author.